



Docket No. ORT-1236 #11

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Zhang et al.  
Serial No. : 09/603,231  
Filed : June 26, 2000  
Title : NOVEL INDOLE PEPTIDOMETICS AS THROMBIN  
RECEPTOR ANTAGONISTS  
Art Unit : 1634  
Examiner : Chakrabarti, Arun K.

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Hal B. Woodrow  
(Name of applicant, assignee, or Registered Representative)

Hal Woodrow  
(Signature)

August 13, 2002  
(Date of Signature)

Honorable Commissioner of Patents  
Washington, D.C. 20231

**RESPONSE**

Dear Sir:

This paper is responsive to the Office Action of February 13, 2002.

**REMARKS/ARGUMENTS**

Claims 1-8, 10 and 11 remain in this application.

Applicants note as a formal matter that the Examiner did not initial the 1449 listing US Patent 6,017,890. Although it is obvious that the Examiner has consider this document, applicants would respectfully request that the Examiner initial the 1449 to complete the record and provide a copy of the initialed 1449 to applicants.

The rejection of claims 1-8, 10 and 11 under 35 U.S.C. 103(a) over Forbes et al. (WO 93/18026) and Hoekstra et al. (US Pat. No. 6017,890) has been considered.

Initially applicants note that Forbes describes indole ureas that are 5-HT<sub>1C</sub> receptor antagonists. 5-HT<sub>1C</sub> appears from the literature that applicants could locate to be a serotonin receptor. Applicants fail to appreciate why an antagonist for a 5-HT<sub>1C</sub> receptor would motivate one skilled in the art to modify the structure of the Hoekstra compounds. It appears that the combination of Forbes and Hoekstra would be inappropriate without some teaching or suggestion in the prior art to combine these documents. No motivation to combine the documents has been alleged to exist in the documents of record. Accordingly, applicants respectfully submit that the combination of Forbes and Hoekstra is improper. Consequently the PTO has failed to satisfy its burden of establishing a *prima facie* case of obviousness. Therefore, applicants respectfully requests reconsideration and withdrawal of the rejection of claims 1-8, 10 and 11 under 35 U.S.C. 103(a) over Forbes et al. (WO 93/18026) and Hoekstra et al. (US Pat. No. 6,017,890).

Applicants have screen compounds having PAR-1 activity against other serotonin receptors in a CEREPS screen and seen some activity against 1A and 1B subtype receptors, but 1C subtype receptors have not been tested.

Applicants also submit that Forbes has substantially different indole substitutions from the present invention, in that R<sub>1</sub> and R<sub>3</sub> of the Forbes document are not equivalent to the substituents on the applicants' indole in the same position. For example the R<sub>1</sub> in Forbes is hydrogen or C<sub>1-6</sub> alkyl while the equivalent position of the present invention is a (CH<sub>2</sub>)<sub>m</sub> attached to a unsubstituted or substituted aryl, arC<sub>1-8</sub> alkyl, C<sub>3-8</sub> cycloalkyl, or heteroaryl, where the substituents on the aryl, arC<sub>1-8</sub> alkyl, cycloalkyl or heteroaryl group are independently selected from one or more of halogen, nitro, amino, cyano, hydroxyalkyl, C<sub>1-8</sub> alkyl, C<sub>1-8</sub> alkoxy, hydroxy, C<sub>1-4</sub> alkylcarbonyl, C<sub>1-8</sub> alkoxy carbonyl, fluorinated C<sub>1-4</sub> alkyl, fluorinated C<sub>1-4</sub> alkoxy or C<sub>1-4</sub> alkylsulfonyl. Similarly, R<sub>3</sub> of Forbes is hydrogen or C<sub>1-6</sub> alkyl while the equivalent position of the present invention contains a (CH<sub>2</sub>)<sub>n</sub> attached to an amino, C<sub>1-8</sub> alkylamino, C<sub>1-8</sub> dialkylamino, arylamino, arC<sub>1-8</sub> alkylamino, C<sub>3-8</sub> cycloalkylamino, heteroalkylC<sub>1-8</sub> alkylamino, heteroalkylC<sub>1-8</sub> alkyl-N-methylamino, C<sub>1-8</sub> dialkylaminoC<sub>1-8</sub> alkylamino, -N(C<sub>1-8</sub>alkyl)-C<sub>1-8</sub> alkyl-N(C<sub>1-8</sub>alkyl)<sub>2</sub>, N(C<sub>1-8</sub>alkyl)(C<sub>1-8</sub> alkenyl), -N(C<sub>1-8</sub>alkyl)(C<sub>3-8</sub>cycloalkyl), heteroalkyl or substituted heteroalkyl wherein the substituent on the heteroalkyl is selected from oxo, amino, C<sub>1-8</sub> alkoxyC<sub>1-8</sub> alkyl, C<sub>1-8</sub> alkylamino or C<sub>1-8</sub> dialkylamino. Consequently, applicants respectfully submit that the combination of Forbes and Hoekstra would not render the present invention obvious (if these references were properly combinable). Accordingly, applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. 103(a) of claim 1-8, 10 and 11 over Forbes and Hoekstra.

Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

Respectfully submitted,

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